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## EDITORIAL

### PENICILLIN

The introduction of a new chemotherapeutic agent in the treatment of gonococcal infection, within a relatively short period since the arrival of the sulphonamides, is an event of the greatest interest. That the newcomer is said to possess an efficiency far above that inherent in any of the sulphonamide compounds is somewhat startling, but the information that this high potency is accompanied by a complete absence of toxicity is, on first acquaintance, almost beyond belief.

The high antibacterial quality of penicillin in the pyogenic infections of some war wounds, and in some other infections, has received much publicity in both the medical and the lay press. The astonishing efficiency and speedy action of this substance, it is reported, is not limited to the common pyogenic cocci but includes in its range other organisms, in one of which—the gonococcus—we have a special interest.

It is therefore with considerable pleasure that we publish in this issue of the *Journal* a brief but interesting account of the first realization of the outstanding antibacterial properties of penicillin from the pen of its discoverer, Sir Alexander Fleming. Some of our readers have had the pleasure of listening to Sir Alexander's modest but enthralling account of his discovery, at a meeting of the Medical Society for the Study of Venereal Diseases in May of this year. Those readers who were unable to be present, but who follow the story elsewhere in these columns, will not fail to recognize that Sir Alexander's acumen in 1929 laid the foundations of the development of a chemotherapeutic agent which has become of importance to the whole human race.

Much extensive and laborious research has since been done by others, notably Sir Howard Florey and his Oxford colleagues, who have succeeded in concentrating and purifying the active principle of the crude culture of penicillin to a degree at which, when it is used in the treatment of human infections, its antibacterial action becomes effective and its toxicity of no import.

Penicillin seems to possess a curative action of a degree of potency much in advance of anything hoped for a few years ago. The earlier extracts were found to be bacteriostatic for sensitive bacteria at the dilution of one in one million, but now the more purified extract is capable of preventing the growth of some bacteria in a dilution of one in fifty million.

The extract of penicillin, although possessing the great advantage of reasonable solubility, is relatively unstable and is susceptible to alterations in pH. Thus the active principle is destroyed by acids, alkalis or heat. It is therefore unsuitable for oral or rectal administration and to be effective must be given parenterally. Various methods, including continuous intravenous drip and intramuscular injection at from three-hourly to four-hourly intervals, have been used and tolerated with excellent results. In the treatment of gonorrhoea these limitations of the method of administration may prove to be no disadvantage, for irregular or inadequate dosage is much more frequently encountered in oral therapy, which is usually dependent upon the patient, than in parenteral treatment.

The astonishingly efficient antibacterial properties of penicillin exhibited *in vitro* in high dilution against cultures of the pyogenic cocci were even surpassed, in experiments by Sir Alexander Fleming, by its action upon cultures of gonococci.

This antibiotic seems to possess fundamental characters of outstanding practical value. For example, the extracts successfully inhibit the growth of some bacteria

in astoundingly high dilutions. It differs from conventional antiseptics in that its activity is not affected by the presence of serum, blood or pus ; in addition it appears to be entirely devoid of any deleterious action upon the structures and cells of the human body. If this be so, it clearly attains ideals that have long been postulated for the perfect antiseptic. Many mould extracts are known to possess powerful antibacterial properties, but the extract of *Penicillium notatum* appears to be unique in also being innocuous to the body tissues. It has been shown that the white blood cells are unaffected by concentrations much greater than those adequate to interfere with the growth of sensitive organisms.

That the practical value of penicillin in combating gonococcal infection would be found to exceed our most sanguine expectation was suggested by the early reports emanating last year from the United States of America and from the British Army in North Africa. Although these early reports dealt with a small number only of cases of gonorrhoea in men, the strikingly favourable results gave some encouragement to the view that a new era of treatment for gonorrhoea might be beginning ; for these preliminary reports indicated that, whatever its value may be in effecting a complete and permanent cure, there seemed to be no doubt about its initial success in terminating all symptoms and signs of gonorrhoea within a matter of hours. Additional reports from the United States of America, which support these early claims, appear to indicate that penicillin therapy effects a real cure in acute recent gonococcal infections in a very high proportion of cases. Furthermore, this curative action is said to be attained just as often in those patients in whom sulphonamide therapy has failed as it is in the previously untreated patient. This property of penicillin of high efficiency in sulphonamide-resistant gonorrhoea should be of the utmost value at the present time, when these sulphonamide-resistant cases, according to numerous reports, appear to have become even more frequent. The susceptibility of sulphonamide-resistant organisms to penicillin has also been shown in cases of pneumococcal meningitis, of staphylococcal bronchopneumonia and of empyema of streptococcal or staphylococcal origin. Dr. Suchet, from his experience in the treatment of some sulphonamide-resistant cases of gonorrhoea (see p. 136), suggests that sulphonamide-resistant gonococcal infection may respond to penicillin even more readily than does the previously untreated infection.

It was a sensible decision of the Ministry of Health, when issuing instructions on the use of penicillin prior to the release of a modest quota of this preparation to civilian hospitals, to include in their second list ("conditions deserving special consideration, which may be treated if supplies are sufficient") cases of gonorrhoea which have been found resistant to initial treatment with sulphonamide compounds. No doubt much time will be saved if such cases can be identified by laboratory methods before treatment is begun ; for the basal technique of ascertaining in the laboratory the vulnerability or resistance to sulphonamides of various strains of gonococci, we are again indebted to Sir Alexander Fleming.

It is to be hoped, when adequate supplies of penicillin become available, that the indiscriminate and unscientific use of drugs that has characterized the era of chemotherapy with sulphonamides will not be repeated. The supply and distribution of penicillin will need control for a considerable period until the volume of supply is large enough to meet all demands. One hopes that the control of supply will be ultimately beneficial and will promote the intelligent and appropriate use of this valuable compound.

The status of the use of penicillin in the treatment of syphilis is one of keen interest. Preliminary investigations of its effects on this disease in rabbits are said to yield excellent results. The use of the compound in the treatment of primary syphilis in man is stated to have resulted in the rapid disappearance of *Spirochaeta pallida* and in the speedy healing of chancres ; the positive serological reactions were said to be reversed to negative at a satisfactory rate. However, much more evidence is required before any useful comment can be made. Meanwhile we are awaiting the results of long-term studies, which may prove that penicillin will soon have a great part to play in the treatment of early syphilis.